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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,325	07/12/2004	Andreas Finke	RDID01062CUS	8527

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EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/774,325	FINKE ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment, filed 10/6/05 is acknowledged. Claims 4 and 6-8 have been cancelled. Claims 1-3 and 5 are currently pending.

Information Disclosure Statement

The information disclosure statement filed February 10/6/05 has been received. The reference by Lagaly, G., et al. has not been considered as it is a German language document.

Election/Restrictions

Applicant's confirmation of the election **without traverse** of Group I, claims 1-5 in the reply filed on 10/6/05 (p. 7) is acknowledged.

Rejections Withdrawn

The objections to the specification are withdrawn in light of Applicant's amendments.

The objections to the drawings are maintained because the replacement drawings submitted 10/6/05 have not been entered (see below).

The rejection of claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Vaynberg et al. are withdrawn in light of Applicant's amendments.

The rejections of claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Jolley et al. are withdrawn in light of Applicant's amendments.

The rejections of claims 3 and 5 under 35 USC 103(a) as being unpatentable over Jolley et al. in view of Tischer et al. and Jolley et al. in view of Bangs, respectively, are withdrawn in response to Applicant's arguments and amendments to claim 1.

The rejection of claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Ortega Vinuesa et al. is withdrawn in light of Applicant's amendments and arguments.

The rejection of claims 1-2 under 35 USC 103(a) as being unpatentable over Amiral in view of Steele is withdrawn in light of Applicant's amendments and arguments.

Drawings

Applicant's amendment included replacement drawing sheets. However, as indicated in the Notice of Non-Compliant Amendment mailed 10/14/05, the replacement drawings are not properly identified as "Replacement Sheet" or "New Sheet" as required by 37 CFR 1.121(d). The amendments to the drawings have therefore not been entered

The drawings filed 7/12/04 are objected to as failing to comply with 37 CFR 1.84(p)(5) because they do not include the following reference sign(s) mentioned in the description: the labels "Figure 1," "Figure 2," "Figure 3," and "Figure 4" are not present in the drawings. In addition, Figure 1 contains text that is not legible: the label designating the Y-axis of the graph is not legible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure

must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-3 and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "the combination" in part (a). There is insufficient antecedent basis for this limitation in the claim.

As suggested in the previous office action, "the microparticle-protein combination" or similar terminology may be employed to indicate that the combination of microparticles and protein is being referred to, with the caveat that the terminology should not introduce new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vaynberg et al. (Vaynberg, K.A., Wagner, N.J., and Sharma, R. (2000) "Polyampholyte Gelatin Adsorption to Colloidal Latex: pH and Electrolyte Effects on Acrylic and Polystyrene Latices," *Biomacromolecules* **1**, 466-472), and as evidenced by Bocquier et al. (Bocquier AA, Potts JR, Pickford AR, Campbell ID (1999) "Solution Structure of a Pair of Modules from the Gelatin-Binding Domain of Fibronectin," *Structure* 7:1451-1460) and by Bohidar ("Hydrodynamic properties of gelatin in dilute solutions" (1998) *International Journal of Biological Macromolecules* **23**:1-6).

Vaynberg et al. teach a method for producing protein-coated polystyrene microparticles that includes the steps of combining a suspension (colloid) of uncoated microparticles with a polymerized protein that is a member of a bioaffinity binding pair (gelatin), the combination

comprising a buffer of pH 10, incubating the combination for a period of time whereby the protein is coated onto the microparticles by adsorption, and separating the non-adsorbed protein from the protein-coated microparticles (by centrifugation) (see p. 467, column 2, lines 30-32 and the section "Materials," lines 9-16; p. 468, column 1, lines 1-4, 15-31, and Table 1; p. 469, column 1, lines 1-7, and column 2, lines 25-29; and p. 470, Figure 8).

The protein gelatin is a partner of a bioaffinity binding pair as it binds fibronectin (see Bocquier et al., p. 1451, column 2, lines 1-10). Gelatin has a size within the recited range of 10 nm to 300 nm as evidenced by Bohidar, in particular at p. 4, Table 2. Bohidar evidences that gelatin has a size within the recited parameters since the radius values reported therein are in the recited range. In particular, the hydrodynamic radius $R_{e,D}$ is 190-280 Å, which is equivalent to 19.0-28.0 nm (Table 2).

Vaynberg et al. do not specifically recite a buffer of pH 10.5 to 12.5. Rather, Vaynberg et al. teach adsorption of gelatin onto the polystyrene particles at various pH values up to pH 10 (Figures 1-7). However, MPEP 2144.05 notes that:

> ...a prima facie case of obviousness exists where the claimed ranges and prior art ranges do not overlap but are close enough that one skilled in the art would have expected them to have the same properties. Titanium Metals Corp. of America v. Banner, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985)

and further that:

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

In the instant case, it would have been obvious to one of ordinary skill in the art to employ slightly higher pH values (for example, pH 10.5) through routine optimization/ experimentation of the conditions of Vaynberg et al. with a reasonable expectation of success. In addition, one would be motivated to employ higher pH values because Vaynberg teaches that because hydrophobic effects dominate in adsorption of gelatin, increasing pH results enables a denser layer of gelatin to form on the polystyrene (p. 470, left, column, first full paragraph).

One would have reasonable expectation of success in employing higher pH values in the method of Vaynberg et al. because Vaynberg et al. repeatedly teach that pH differences were not critical and produced *little variation in the adsorption efficiency* of gelatin onto the polystyrene (p. 469, right column, line 25 to p. 470, left column and Figures 2-3). In particular, Vaynberg et al. teach that "pH hardly affects the adsorption of gelatin to [polystyrene]" (p. 470, left column, lines 12-13) and further note "the ability of gelatin to adsorb to [polystyrene] even at high electrolyte and high pH conditions" (p. 471, right column, second paragraph).

3. Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vaynberg et al. as evidenced by Bocquier et al. and Bohidar as applied to claim 1 above, and in view of Tischer et al. (US Patent No. 5,061,640).

Vaynberg et al. is as discussed above, which fails to teach a protein that has been polymerized by chemical treatment.

Tischer et al. teach a process for the preparation of a protein for adsorption to an insoluble carrier material such as polystyrene (see column 2, lines 25-34 and column 4, lines 19-38). In particular, Tischer et al. teach polymerizing of proteins to be adsorbed using a cross-linking compound (column 3, lines 32-39 and 63-68; column 4, lines 1-7; column 8, Example 2,

lines 38-42; and column 9, part (d), lines 9-10). Tischer et al. further teach that this polymerizing of proteins has the effect of increasing their molecular weights (column 3, lines 32-43), which results in improved adsorption of the proteins to the insoluble carrier material (see column 2, lines 35-37).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include the step of polymerizing gelatin by treatment with a cross-linking compound, as taught by Tischer et al., in the method for producing protein-coated microparticles of Vaynberg et al. in order to increase the molecular weight of gelatin and thereby improve the adsorption of gelatin to polystyrene. One would have reasonable expectation of success because Tischer et al. teach the step of increasing the molecular weight in preparation for coating proteins onto polystyrene by adsorption, which is the object of the method of Vaynberg et al.

4. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vaynberg et al. as evidenced by Bocquier et al. and Bohidar as applied to claim 1 above, and in view of Desai et al. (US 6,638,728 B1).

Vaynberg et al. fail to teach a method where the protein coated is streptavidin that has been polymerized by chemical treatment.

Desai et al. (US 6,638,728 B1) teach methods for producing surfaces such as polystyrene spheres that are coated with streptavidin that has been polymerized by treatment with a chemical cross-linking reagent, (see in particular column 1, lines 25-30 and 60-67; column 2, lines 17-34; column 2, line 65 to column 3, line 24). Desai et al. teach that such surfaces are in capturing target molecules in assays (column 1, lines 53-59).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the method for producing protein-coated polystyrene microparticles of Vaynberg et al. to coat streptavidin that has been polymerized by chemical treatment, as taught by Desai et al. in order to produce microparticles that have a high capacity for capturing target molecules for use in assays. One would have reasonable expectation of success in employing the method of Vaynberg et al. with the polymerized streptavidin taught by Desai et al. because Desai et al. teach that polystyrene, which is the material taught in Vaynberg et al., is an appropriate solid phase for immobilization of polymerized streptavidin (see Desai at column 3, lines 42-44). In addition, while Vaynberg et al. only specifically teach the protein gelatin, Vaynberg et al. teach the adsorption of polyampholytes such as proteins in general (see p. 466, left column, first two paragraphs; and p. 471-472, "Conclusions").

5. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Vaynberg et al. as evidenced by Bocquier et al. and Bohidar as applied to claim 1 above, and further in view of Bangs ("New developments in particle-based immunoassays: introduction" (1996) *Pure & Appl. Chem.* **10**:1873-1879). Vaynberg et al. is as discussed above, which fails to teach microparticles that have a magnetizable core.

However, Bangs teaches microparticles that have a magnetizable core (superparamagnetic particles and magnetic microspheres; see p. 1873, "Introduction," lines 1-4 and p. 1876, "Superparamagnetic Particle Based Assays") and their utility in fast and easy separation of solid and liquid phases.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to include the microparticles having a magnetizable core as taught by Bangs in the

method for producing protein-coated polystyrene microparticles of Vaynberg et al. because Bangs teaches the convenience of such microparticles in the fast and easy separation of solid and liquid phases in various assay types, including RIA, ELISA, and immunoradiometric assays.

Response to Arguments

Applicant's amendments and arguments in the amendment filed 10/6/05 have been fully considered.

The rejection of claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Vaynberg et al. has been withdrawn in response to Applicant's amendment of claim 1 to recite a pH of 10.5 to 12.5. However, the reference has been applied to support the rejection of claims 1-3 and 5 under 35 USC 103(a) above. Applicant argues that gelatin is not a partner of a bioaffinity binding pair as required by the claim (see Applicant's response, p. 10). This argument is not found persuasive because gelatin is a member of the gelatin-fibronectin bioaffinity binding pair, as evidenced by Bocquier et al. as noted above and in the previous office action (p. 10, item 16, the last 4 lines). In particular, Bocquier et al. teach the "gelatin-binding domain of fibronectin" (the title), which is evidence that gelatin binds fibronectin. Applicant provides examples of "bioaffinity binding pairs" in paragraph 29 of the specification, but does not explicitly define the term. As gelatin and fibronectin are biological molecules that bind each other, this meets the limitation of a "bioaffinity binding pair".

With regard to the rejection to claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Jolley et al., Applicant argues that Jolley does not disclose or anticipate the invention recited in claims 1 and 2 as amended (Applicant's response, p. 10, last paragraph to p.

11, second paragraph). Although Applicant provided no specific arguments as to why Jolley is not anticipatory, the rejections are withdrawn in light of Applicant's amendments. In particular, while Jolley et al. teaches a method of producing protein-coated polystyrene microparticles at pH values of 5-10 (Table 1), Jolley et al. does not teach such a method at pH 10.5-12.5.

The rejection of claims 1-2 and 4 under 35 USC 102(b) as being anticipated by Vinuesa et al. is withdrawn in light of Applicant's amendments and arguments (see p. 11-12 of Applicant's response).

The rejection of claims 1-2 under 35 USC 103(a) as being unpatentable over Amiral in view of Steele is withdrawn in light of Applicant's amendments and arguments (see p. 12-13 of Applicant's response).

The rejections of claims 3 and 5 under 35 USC 103(a) as being unpatentable over Jolley et al. in view of Tischer et al. and Jolley et al. in view of Bangs, respectively, are withdrawn in response to Applicant's arguments and amendments. Specifically, Applicant's amendment of claim 1 to recite a pH of 10.5 to 12.5, together with Applicant's argument (p. 14-15 of Applicant's response) that while Jolley teaches a pH range of 5-10, the efficiency of protein adsorption to the particles declines above pH 9 (see Table 1 and p. 27 of Jolley), such that Jolley et al. teaches away from using pH values higher than 10, are persuasive to overcome the rejections.

Bangs is relied upon in the rejection of claim 5 above (see item 5 above, Vaynberg et al. in view of Bangs). Applicant argues with respect to the previous rejection that Bangs does not teach a pH in the claimed pH range (see Applicant's response at p. 15, first paragraph). With regard to the instant rejection, this argument is not persuasive because the Vaynberg et al.

reference is relied upon for this teaching, as discussed above, while the Bangs reference is relied on solely for the teaching of polystyrene microparticles having a magnetizable core.

Conclusion

No claims are allowed.

The following references not relied upon above are also cited by the examiner as prior art of relevance:

Suzawa et al. ("Adsorption of Plasma Proteins onto Polymer Latices" Advances in Colloid and Interface Science (1991) 35:139-172) teaches the absorption of BSA onto polystyrene latex at pH values of 3-11 (see p. 149-150 and 152-156 in particular). In particular, Suzawa teach that at higher ionic strength, adsorption of the protein to polystyrene is *little influenced by pH* (see Figures 8 and 11 and p. 150, third paragraph in particular).

Van Oss et al. ("The binding of immune globulins and other proteins by polystyrene latex particles" (1966) *J. Reticuloendothel Soc.* **3**:29-40) is cited for its teaching that binding of proteins such as human IgG to polystyrene particles was well-known in the art to be "wholly pH independent" (see the abstract). However, Van Oss et al. specifically teach production of IgG-coated polystyrene particles only up to pH 9 (see Figure 3).

Hevey et al. (US 4,228,237) is cited for teaching of coating proteins onto polystyrene surfaces at high pH (pH 9.8; see column 10, lines 58-65).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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